AMENDMENTS TO THE DRAWINGS:

The attached sheets of drawing includes changes to Figs. 3 and 5. These sheets replace the original sheet for Figs. 3 and 5.

As requested by the Examiner, the drawings have been lightened so that the bands can been seen.

REMARKS

FORMAL MATTERS:

Claims 5-8, 21-26 and 28-30 are pending after entry of the amendments set forth herein.

Claims 5, 7, 21, 24, 28 and 29 are amended for clarity. The amendments should generate no new issues for the Examiner and, as such, their entry is respectfully requested. No new matter is added.

In view of the remarks set forth below, reconsideration of this application is respectfully requested.

OBJECTIONS TO THE CLAIMS

Claims 5, 7, 21, 24 and 28 have been objected to by the Examiner for minor informalities.

The minor informalities of Claims 5, 7, 21, 24 and 28 have been corrected by amendment and it is believed that these objections have been addressed.

Withdrawal of these rejections is respectfully requested.

REJECTION OF CLAIMS UNDER 35 U.S.C. §112, ¶2

Claims 5-8, 21-26 and 28-30 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for reciting the phrase: "measuring the ability of the compound or compounds to inhibit or stimulate said receptor". In attempting to establish this rejection, the Examiner argues that the phrase renders those claims indefinite because it is unclear what is being measured.

According to MPEP § 2173[1], the standard for meeting the requirement for definiteness set forth in 35 U.S.C. § 112, second paragraph, is an objective one that requires an analysis of the

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[1] See, e.g., MPEP § 2173.02: "The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of:

(A) The content of the particular application disclosure;

(B) The teachings of the prior art; and

(C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made."

specification, the teachings of the prior art, and how the claim would be read by one of one of ordinary skill in the art. Per MPEP § 2173.02, the claims should *not* be analyzed for definiteness in a vacuum.

The Applicants submit that given the specification and the teachings of the prior art, one of skill in the art would have no trouble understanding what is meant by the phrase "measuring the ability of the compound or compounds to inhibit or stimulate said receptor". For example, given the discussion in the Background section of this patent application, the Applicants submit that one of skill in the art would readily understand that the phrase means measuring coupling to a G protein or a signal that is transduced by the receptor.

The Applicants submit that this rejection has been adequately addressed by the foregoing discussion. Withdrawal of this rejection is respectfully requested.

Claims 5-8, 21-26 and 28-30 are further rejected under 35 U.S.C. §112, second paragraph, as being indefinite for reciting the phrase: "identifying the compound or compounds that inhibit or stimulate said receptor as an agonist, partial agonist, or inverse agonist of said receptor". In attempting to establish this rejection, the Examiner argues that the phrase renders those claims indefinite because the phrase neither states how an agonist, partial agonist or inverse agonist is determined.

In response, the Applicants again refer to MPEP § 2173 (see footnote on previous page) and submit that the terms in question, namely "agonist", "partial agonist" and "inverse agonist" are art recognized terms with well defined meaning. In support of this position, the Applicants respectfully refer the Examiner to pages 29 and 30 Goodman & Gilman's textbook from 1995, which defines those exact terms with no ambiguity.

Given that the terms in question, namely "agonist", "partial agonist" and "inverse agonist" are art recognized terms with well defined meaning, one of skill in the art would have no trouble understanding how they can be determined. The Applicants submit that the use of those terms in these claims should cause no indefiniteness.

The Applicants submit that this rejection has been adequately addressed by the foregoing discussion. Withdrawal of this rejection is respectfully requested.

Claims 28-30 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for reciting the phrase "an endogenous version" because it is allegedly unclear what is meant by that phrase.

In response to this rejection, the Examiner is respectfully referred to the bottom of page 5 of the instant application, where the term "endogenous" is explicitly defined.

Given this definition, one of skill in the art would recognize that the endogenous receptors recited in the rejected claims are receptors that are naturally produced.

The Applicants submit that this rejection has been adequately addressed by the foregoing discussion. Withdrawal of this rejection is respectfully requested.

Claims 28-30 are further rejected under 35 U.S.C. §112, second paragraph, as being indefinite for reciting the phrase "a polynucleotide that hybridizes under stringent conditions to the complement of SEQ ID NO:19, wherein said stringent conditions comprise a wash at 65°C in 0.1xSSC". In attempting to establish this rejection, the Examiner argues that only the wash conditions are given, leaving the hybridization conditions undefined.

In response, the Applicants again refer to MPEP § 2173 (see footnote on previous page) and submit that meaning of the phrase in question would be well known by one of skill in the art.

Nevertheless, solely to expedite prosecution and without any attempt to acquiesce to the correctness of this rejection, the Applicants propose to amend the claim to recite the following: "a polynucleotide that hybridizes to the complement of SEQ ID NO:19 under conditions comprising a stringent wash, wherein said conditions comprise a wash at 65°C in 0.1xSSC."

The Applicants request that the Examiner indicate whether the alternative claim language would be acceptable.

REJECTION UNDER §101

Claims 5-8, 21-26 and 28-30 have been rejected under 35 U.S.C. § 101 as lacking patentable utility. The Applicants respectfully traverse this rejection.

As noted in the Applicant's prior response, the instant specification shows that the GPCR hARE-2 is selectively expressed in an area of the brain - the *substantia nigra* – that degenerates

in Parkinson's disease. The degeneration of the *substantia nigra* is the primary cause of Parkinson's disease.

The Applicants acknowledge that data showing that hARE-2 is selectively expressed in the *substantia nigra* neither proves a causative link between hARE-2 and Parkinson's disease, nor provides the natural ligand for hARE-2. However, neither is necessary for the utilities set forth below.

The selective expression pattern of hARE-2 in *substantia nigra* cells allows for modulation of the intracellular levels of downstream signaling molecules (cAMP, IP_3 and/or Ca^{2+}) *selectively* in those cells. Fluctuations in the intracellular levels of these very same molecules are correlated with the viability of *substantia nigra* cells[2]. Thus, the claimed method can be used to identify compounds that modulate the intracellular levels of molecules that are directly implicated in the survival of those cells. Stated a different way, the claimed method can be used to identify compounds that increase the "well-being" of *substantia nigra* cells and stave off or slow the progression of Parkinson's disease.

This utility relies on well established links, namely: a) that GPCRs modulate the levels of intracellular signaling molecules and b) that the same GPCR-modulated intracellular signaling molecules affect the "well being" of *substantia nigra* cells (see, e.g., the references in footnote 2, below).

In addition, the claimed screening methods can be employed to identify compounds that can be employed in the study, diagnosis or monitoring of Parkinson's disease. For example, a compound identified by the claimed method may be employed in radio-imaging methods for the study of Parkinson's disease, in a similar manner to the compounds as described in Leenders et al. (Arch. Neurol 1990 47:1290-1298) and Fischman et al. (Synapse 1998 29:128-141). This additional utility also exploits the selective expression of hARE-2 in *substantia nigra cells.*

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[2] See, e.g., Hulley et al, Inhibitors of type IV phosphodiesterases reduce the toxicity of MPTP in *substantia nigra* neurons *in vivo*. Eur. J. Neurosci. 1995 Dec 1;7(12):2431-40; and Hirsch et al, Neuronal vulnerability in Parkinson's disease. J Neural Transm Suppl. 1997;50:79-88, as discussed in prior response.

The Applicants submit that both of the above-described utilities are credible, specific and substantial. Since no more is required to meet the requirements of 35 U.S.C. §101, this rejection should be withdrawn.

The Applicants confess to being somewhat perplexed by the Examiner's apparent requirement of disclosure of a ligand for hARE-2, or a causative link between hARE-2 and a motor impairment disorder, in order to conclude that hARE-2 has patentable utility. Neither a ligand nor a causative link is required for the utility described above, and the Applicants are not aware of any court decision or rule that requires a ligand or a causative link before a receptor can become patentable. By analogy, the Applicants submit that the *substantia nigra*-selective expression of hARE-2 makes hARE-2 conceptually no different from a marker for any diseased cell, e.g., HER2, that can be employed to deliver drugs to diseased cells without any knowledge of the actual function of the marker nor knowledge of the ligand to which the marker binds.

It is understood that the Examiner's comments in this Office Action, which largely relate to an asserted lack of a causative link between Parkinson's disease and hARE-2, and the identification of a ligand for hARE-2, have been addressed above.

If this rejection is maintained, the Examiner is requested to explain in more detail the rationale behind the Examiner's reasoning that the asserted utility – the use of the claimed method to identify compounds for treating Parkinson's disease and other diseases caused by degeneration of the *substantia nigra* – is thought to be neither specific nor substantial, as indicated on page 5 of the Office Action. To be specific, the Applicant's cannot see the conceptual difference between Parkinson's disease and other diseases, e.g., breast cancer or HIV, that renders Parkinson's disease non-specific and insubstantial. Clarification is requested.

The Applicants submit that this rejection has been adequately addressed. Withdrawal of this rejection is respectfully quested.

REJECTIONS UNDER §112, ¶1 (ENABLEMENT)

Claims 5-8, 21-26 and 28-30 are rejected as not meeting the enablement requirement of 35 U.S.C. § 112, first paragraph.

The basis for this rejection is the Examiner's contention that the claims are not supported by a patentable utility.

As such, it is believed that this rejection has been adequately addressed in the discussion in the preceding section of this response.

In view of the discussion in the preceding section of this response, this rejection may be withdrawn.

REJECTIONS UNDER §112, ¶1 (WRITTEN DESCRIPTION)

Claims 28-30 are rejected as not meeting the written description requirement of 35 U.S.C. § 112, first paragraph. The Applicants respectfully traverse this rejection.

Claims 28-30 recite "a G protein-coupled receptor consisting of the polypeptide of SEQ ID NO:20 or an endogenous version thereof which is encoded by a polynucleotide that hybridizes under stringent conditions to the complement of SEQ ID NO:19".

In attempting to establish this rejection, the Examiner notes that the specification provides only a single representative species (SEQ ID NO:20), and contends that because the specification provides a single representative species, the genus of polypeptides recited in the claims is inadequately described. The Examiner cites *Lilly*[3], as the sole support for this rejection.

The Applicants submit that the written description requirement of 35 U.S.C. §112, first paragraph, does not require a description of the complete structure of every species within a chemical genus, particularly when one of skill in the art would not expect substantial variation within those species.[4]

Claims 28-30 recite a genus of G protein-coupled receptors (GPCRs) that includes the GPCR of SEQ ID NO:20, and other *endogenous* GPCR that are encoded by a polynucleotide that

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[3] *Regents of the University of California* v. *Eli Lilly & Co.*, 119 F3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997)

[4] See, e.g., *Utter v. Higara* 845 F.2d 993, 998, 6 USPQ 1709, 1714 (Fed. Cir. 1998) ("A specification may, within the meaning of 35 U.S.C. §112, ¶1 contain a written description of a broadly claimed invention without describing all species the claim encompasses."). See also *Enzo Biochem*, 296 F.3d 1316, 63 USPQ2d 1602 (Fed. Cir. 1998) and Examples 9 and 13 of the "Synopsis of Application of Written Description Guidelines", as published to the world wide website of the U.S.P.T.O. on March 1st, 2000.

hybridizes to SEQ ID NO:19 (which encodes SEQ ID NO:20). The Examiner's attention is drawn to the words in italics – the GPCRs recited in the claim are *endogenous*.

In view of the definition of "endogenous" as discussed above, claims 28-30 therefore recite a G protein coupled receptor (GPCR) that consists of SEQ ID NO:20, or a different, *naturally-produced* GPCR that is encoded by a polynucleotide that hybridizes to SEQ ID NO:19 (which encodes SEQ ID NO:20).

Therefore, the GPCRs recited in the rejected claims are: a) naturally produced and b) encoded by a polynucleotide that hybridizes to SEQ ID NO:19. Given this, one of skill in the art would not expect the incredibly broad range of variation the Examiner seems to read into the claim.

For example, with respect to natural variants, one of skill in the art would not expect substantial structural variation among species encompassed within the scope of the claims. This assertion is supported by, e.g., entries into the so called "GPCR natural variants database" (see http://nava.liacs.nl/index.html) which lists the amino acid sequences of many GPCRs and their natural variants. According to this database, (see., e.g., the variation in the D(1A) dopamine receptor found at http://nava.liacs.nl/cgi-bin/result_page_general.py?acc=P21728, natural variants of a GPCR often have amino acid substitutions at a *single* position within the GPCR. Thus, the expected structural variation of naturally produced GPCRs recited in the rejected claims is not substantial.

Since one of skill in the art would not expect substantial structural variation among species encompassed within the scope of the claims, the Applicants submit that the genus is adequately described by disclosure of a single species.

The Applicants note that withdrawal of this rejection would be consistent with recent decisions by the Board of Patent Appeals and Interferences of the United States Patent and Trademark Office. The decisions are and *Ex parte Bandman* BAPI Appeal No. 2004-2319 (2004) and *Ex parte Sun* BAPI Appeal No. 2003-1993 (2003), among others. The genus claims that are the subject of in these decisions were supported by disclosure of a *single* representative species encompassed by the claims.

The Applicants submit that this rejection has been adequately addressed. Withdrawal of this rejection is respectfully requested.

CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number AREN-011CON.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: February 20, 2007

By: _____
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